

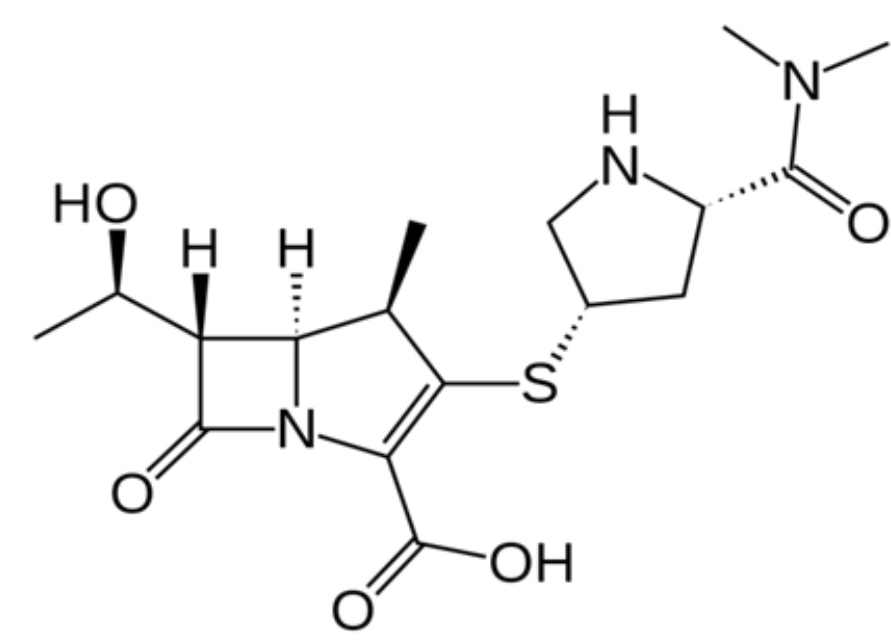
INTRODUCTION

Meropenem is a broad-spectrum antibiotic used to treat severe infectious. The maximum dose recommended is **6 g** per day. A stability not exceeding 24 h has been demonstrated by many research teams in different publications. Only 2 studies were performed **at 40 mg/mL in polypropylene syringes with conflicting stability results: 4h and 8h.** [1] [2] **Meropenem** is a time-dependent antibiotic, its **continuous administration** improves its efficiency.

PURPOSE

To study the **physicochemical stability** of **meropenem** to prepare 3 syringes of 2 g every 8 hours in a **minimum injection volume**.

- **Concentration:** 41.7 mg/mL (2 g in 48 mL)
- **Container:** polypropylene syringe
- **Solvent:** 0.9% sodium chloride (0.9% NaCl) or Dextrose 5 % (D5W)
- **Storage:** 20-25 °C, not protected from light
- **Analysis time:** H0, H4 and H8



MATERIALS AND METHOD

CHEMICAL STABILITY

Method: RP-HPLC with DAD detector at 297 nm [3]

- C18 LiCrospher® 12.5 cm, particule size = 5 µm
- **Mobile phase:** isocratic: ammonium acetate buffer (10 mM) / acetonitrile 95/5 (v/v), pH = 3.0 adjusted with HCl 0.1M
- **Flow rate:** 1mL/min
- **Injection volume:** 20 µL

→ **VALIDATION ACCORDING TO THE ICH Q2(R1)**

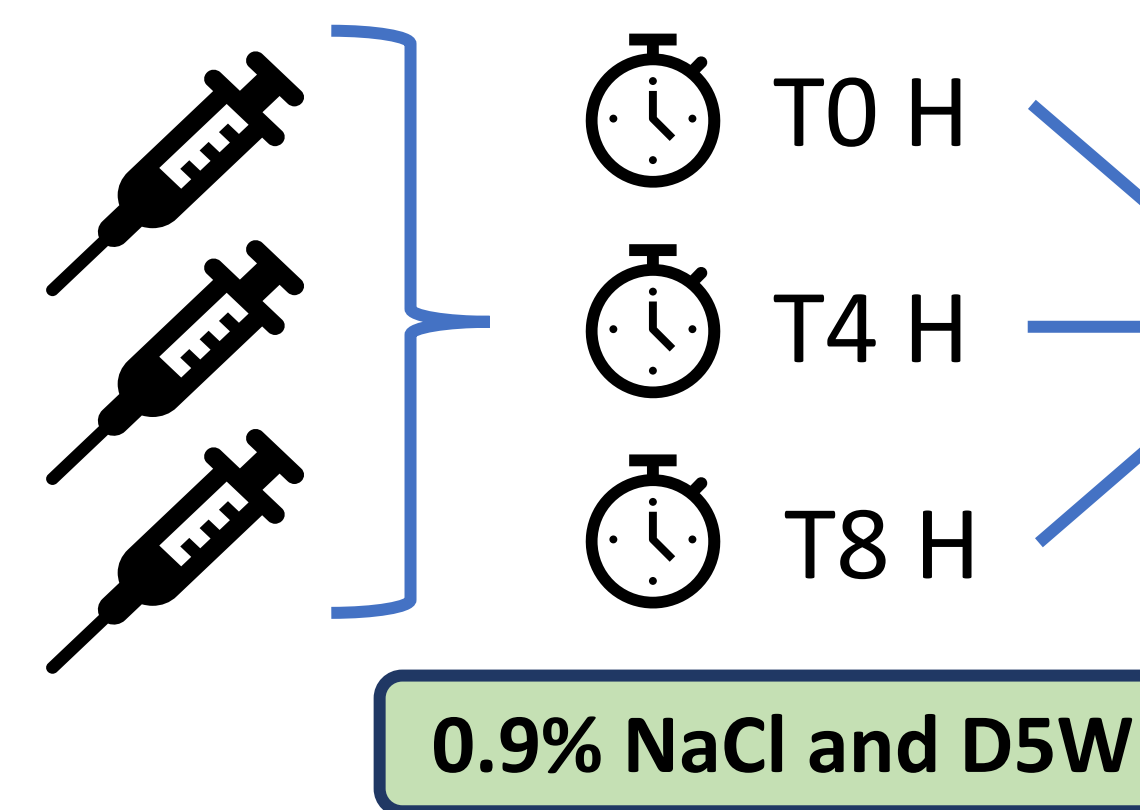
- **Forced degradation:** HCl 0.1M (10 min); NaOH 0.01 M (20 min); UV (1h at 254 nm); heat (1h at 50°C)
- **Linearity:** standard curve with 5 points: between 50 to 250 µg/mL
- **Repeatability and intermediate precision:** 50, 150, 250 µg/mL
- **pH measurement** (Bioblock Scientific pH meter)

PHYSICAL STABILITY

Visual inspection: search for colour change, precipitation and gaz formation

Subvisual inspection: turbidimetry by spectrophotometry at 350, 450 and 550 nm (Safas Monaco UV m²)

STUDY DESIGN



- **Analysis by HPLC:** concentration and degradation products: 3 samples by syringe
- **pH measurement**
- **Visual inspection**
- **Subvisual inspection**

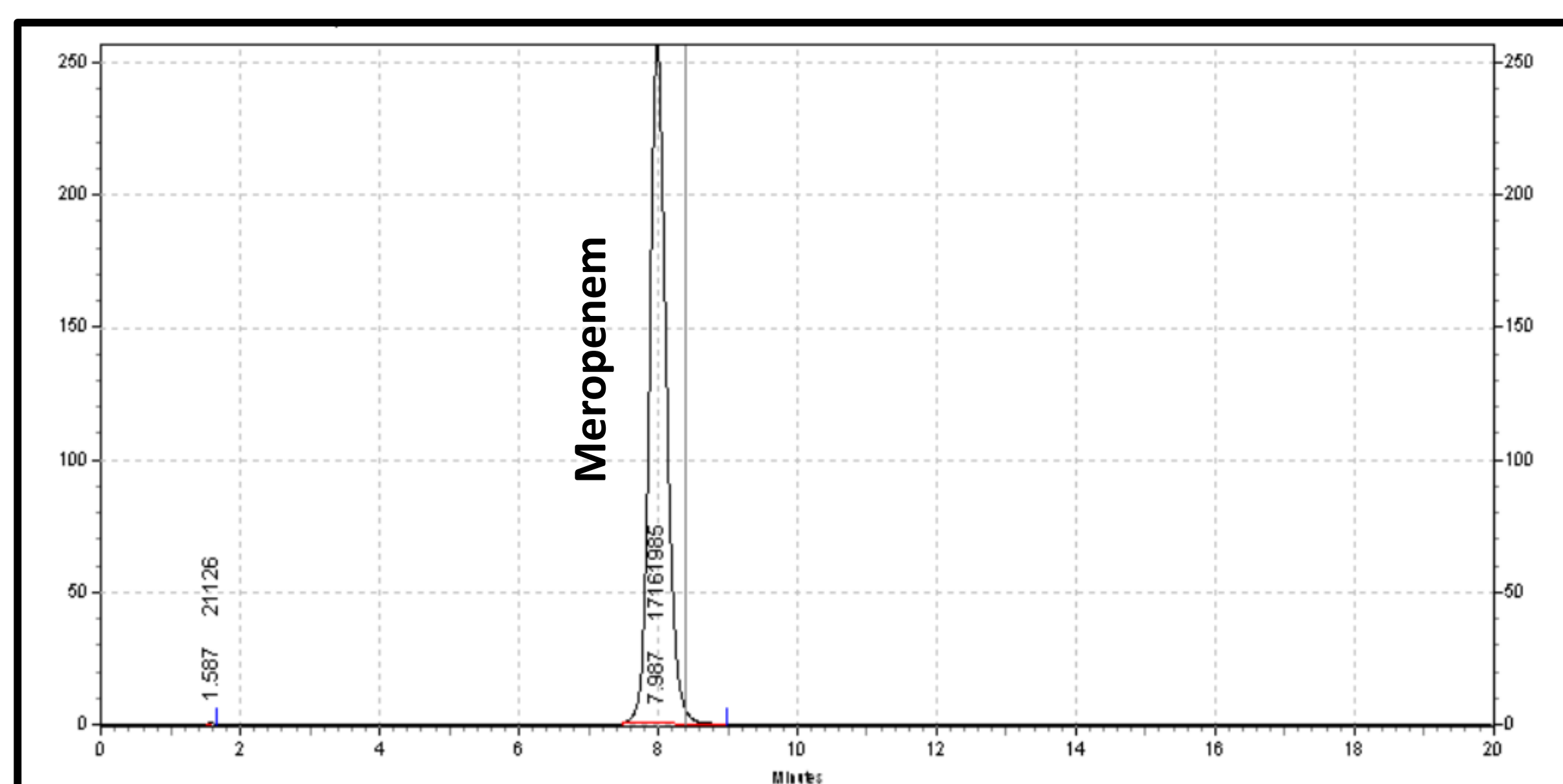
Agreement of STABILITY:

- ± 10% of the initial concentration
- no significant subvisual, visual and pH variation

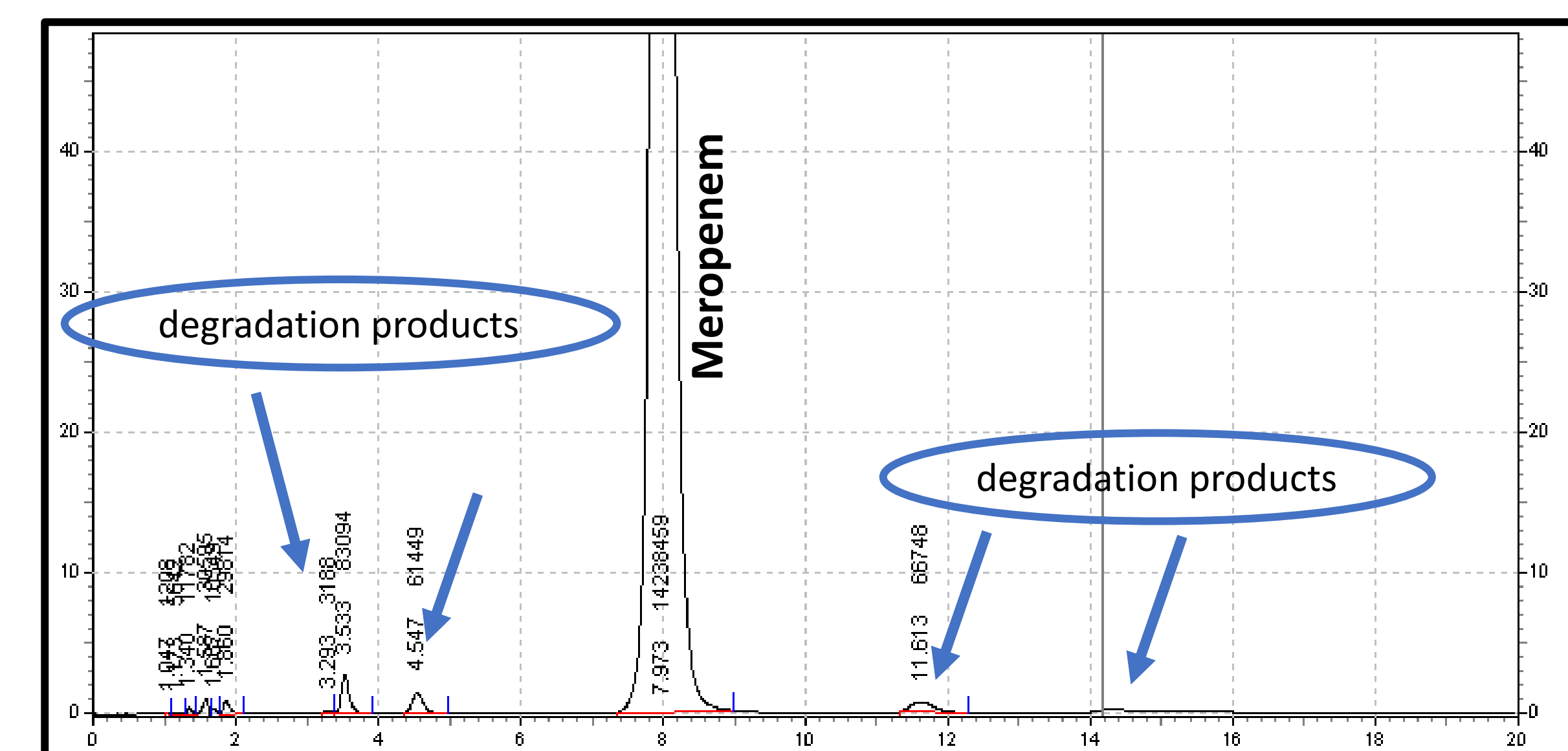
RESULTS

① Validation: RP-HPLC method

- **Linearity :** R² > 0.9999
- **Repeatability and intermediate precision :** CV < 2%
- **Retention time:** 7.9 min
- **Stability indicating capacity :**

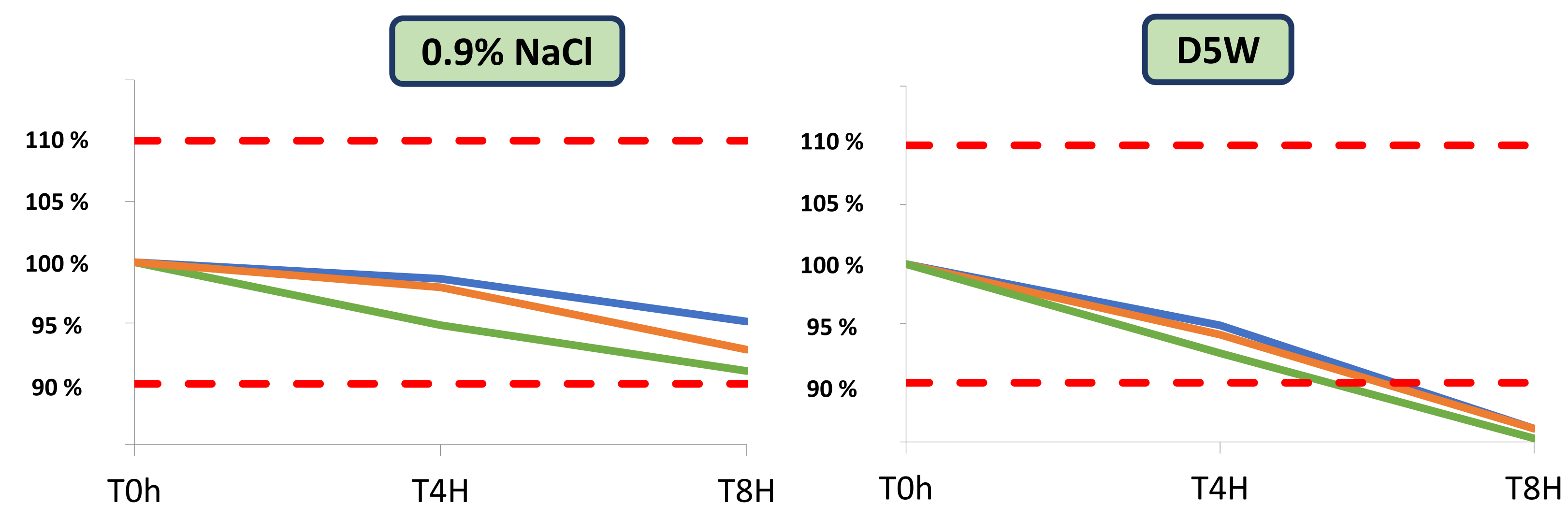


Chromatogram of meropenem 150 µg/mL in 0.9% NaCl without stressed conditions



Chromatogram of meropenem 150 µg/mL in 0.9% NaCl after photolysis degradation (UV 254 nm, 1h)

② Chemical stability HPLC :

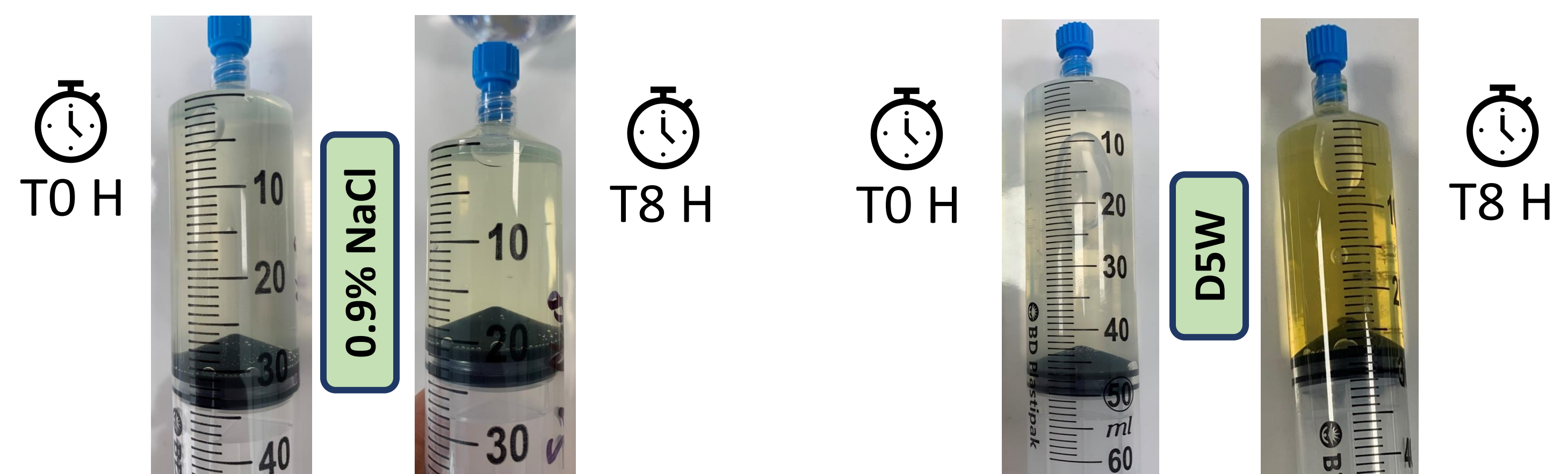


Room temperature (20-25 °C) not protected from light

- **pH measurement :** decreased slightly with maximum variation : 0.2 unit pH (7.8 → 7.6), T0h → T8h in **D5W** and 0.15 pH unit in **0.9% NaCl**

③ Physical stability :

- **Subvisual inspection:** no significant variation in **0.9% NaCl**. In the **D5W** at 410 and 550 nm, major increase in absorbance between T0h and T8h.
- **Visual inspection:** major colour change in **D5W** (yellowing +++) at T4 h and T8h. In **0.9% NaCl** only slight intensification in colour was observed.



CONCLUSION



Meropenem was **stable** at **41.7 mg/mL** in **polypropylene syringes** diluted in **0.9% NaCl** for **8 hours**. This new stability data allows a **continuous administration**.



In **D5W** **meropenem** was **unstable**, with chemical and physical instability.